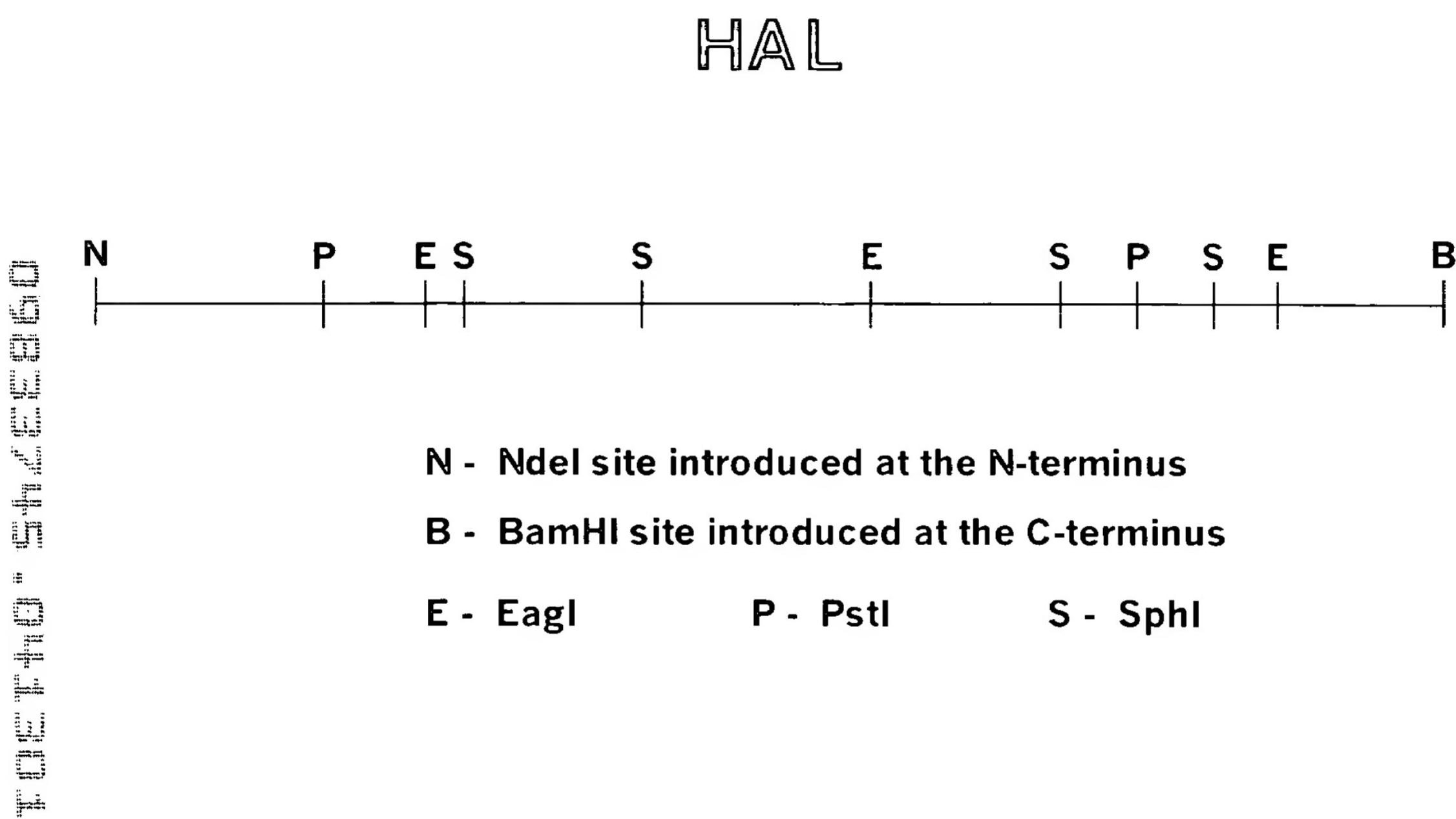


Figure 1: Restriction pattern of the HAL coding region cut with selected enzymes.



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Figure 2: Experimentally derived peptide sequences of HAL

N-terminal

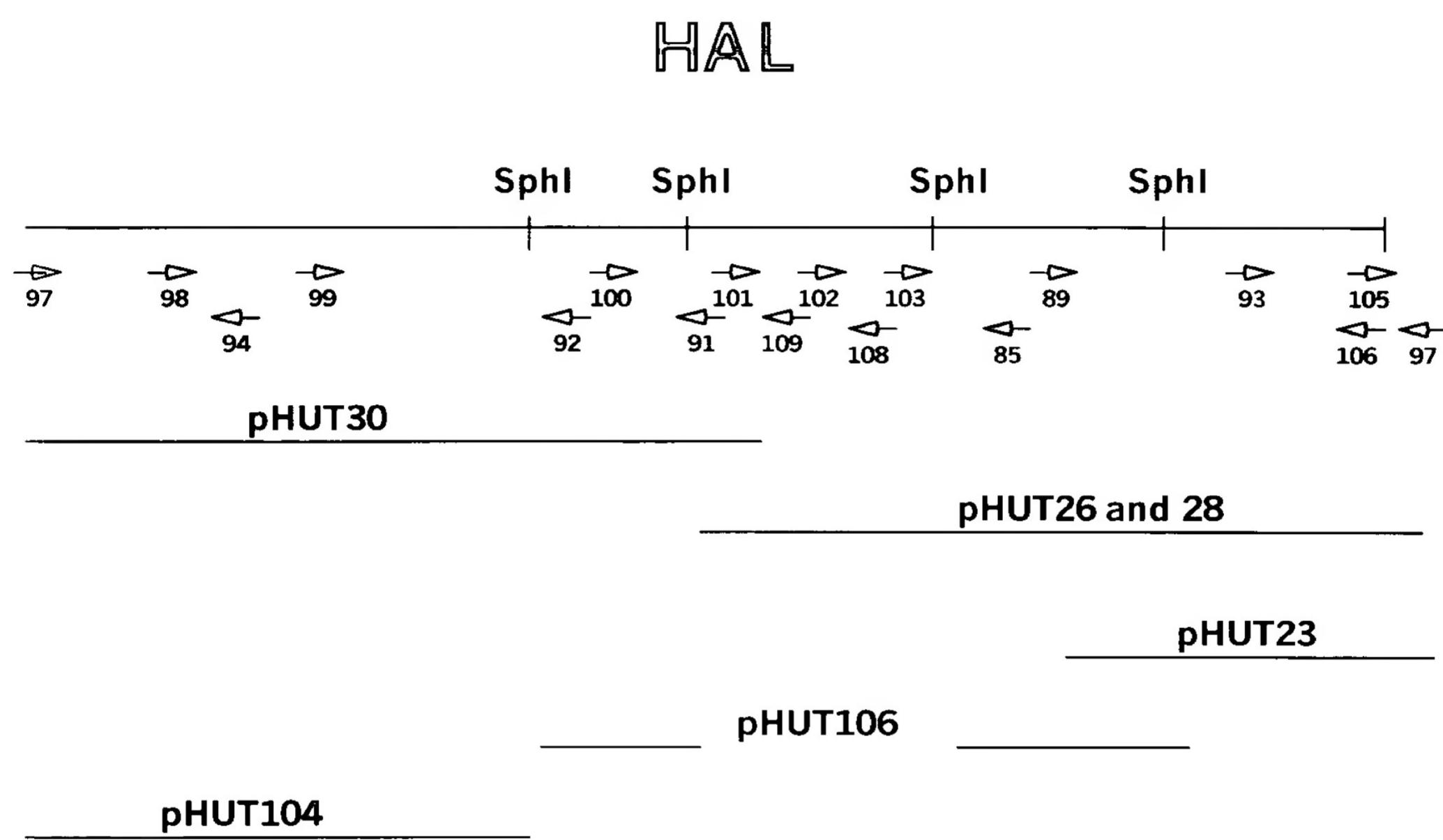
(M)ASAPQITLGLSGATAD

Internal

(M)ALADLDELLDEA

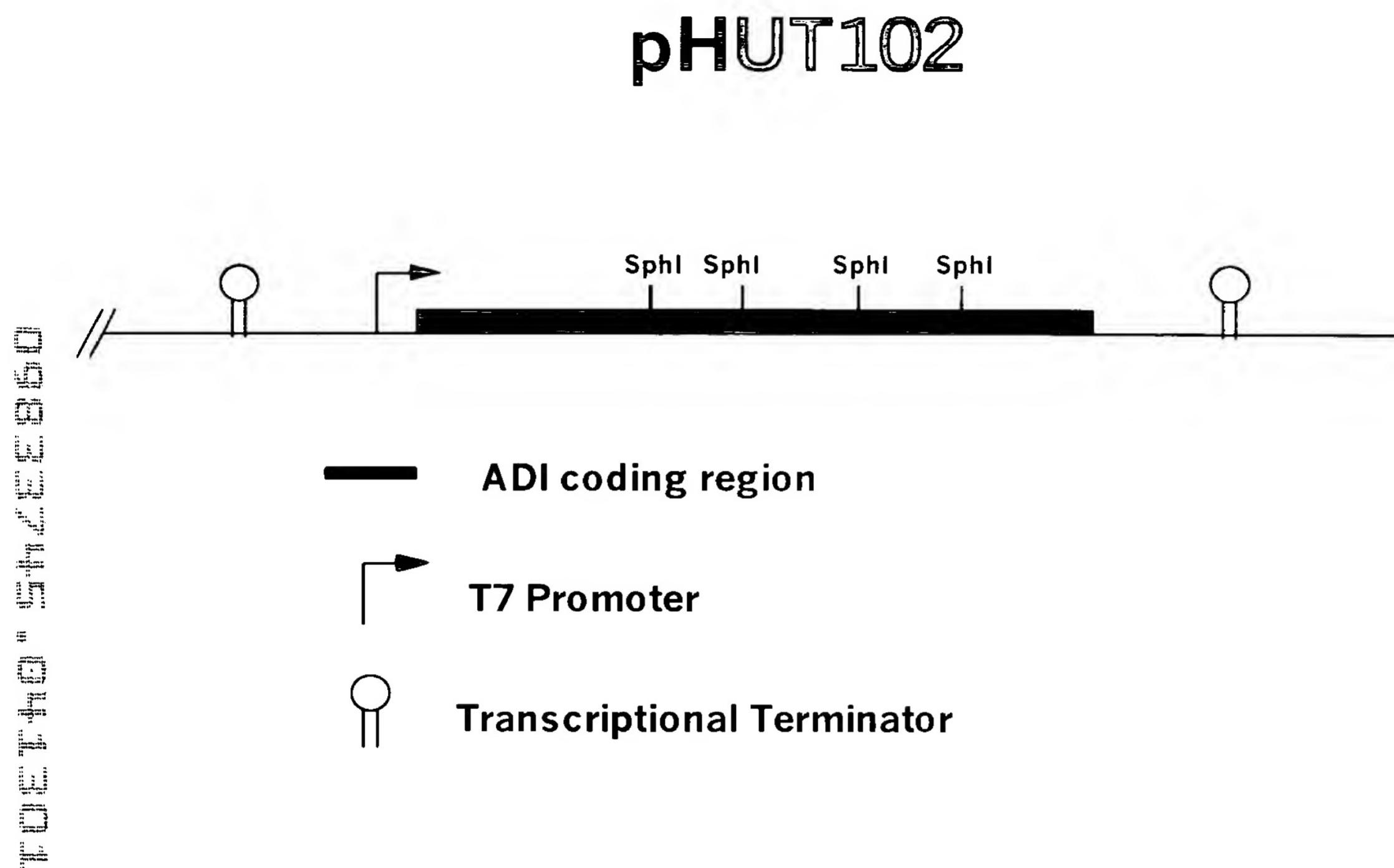
(M)GEPVEREVLRA

Figure 3: SphI digestion pattern of HAL gene showing oligonucleotide and subclones.



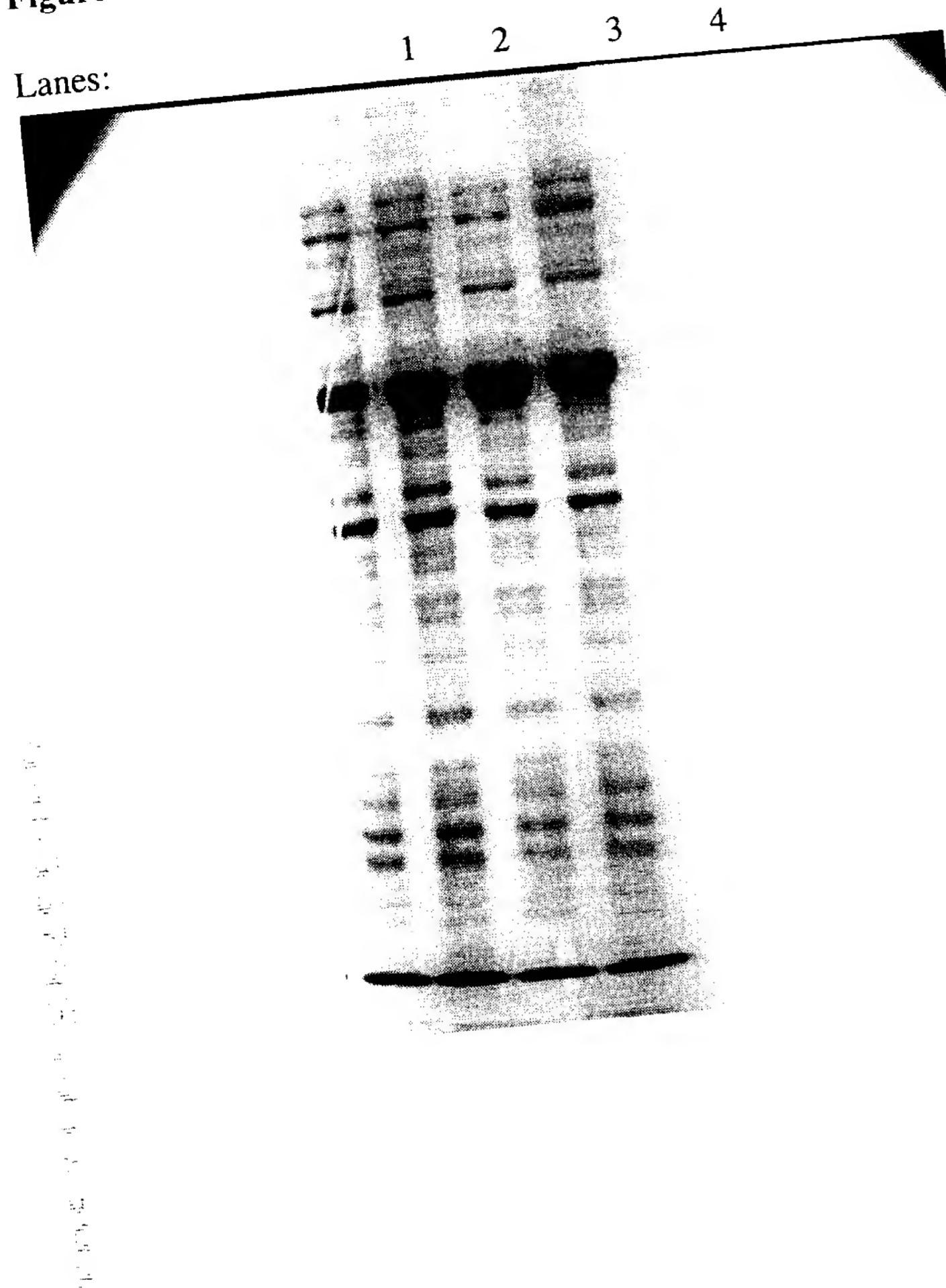
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Figure 4: Histidine ammonia lyase overexpressing plasmid.



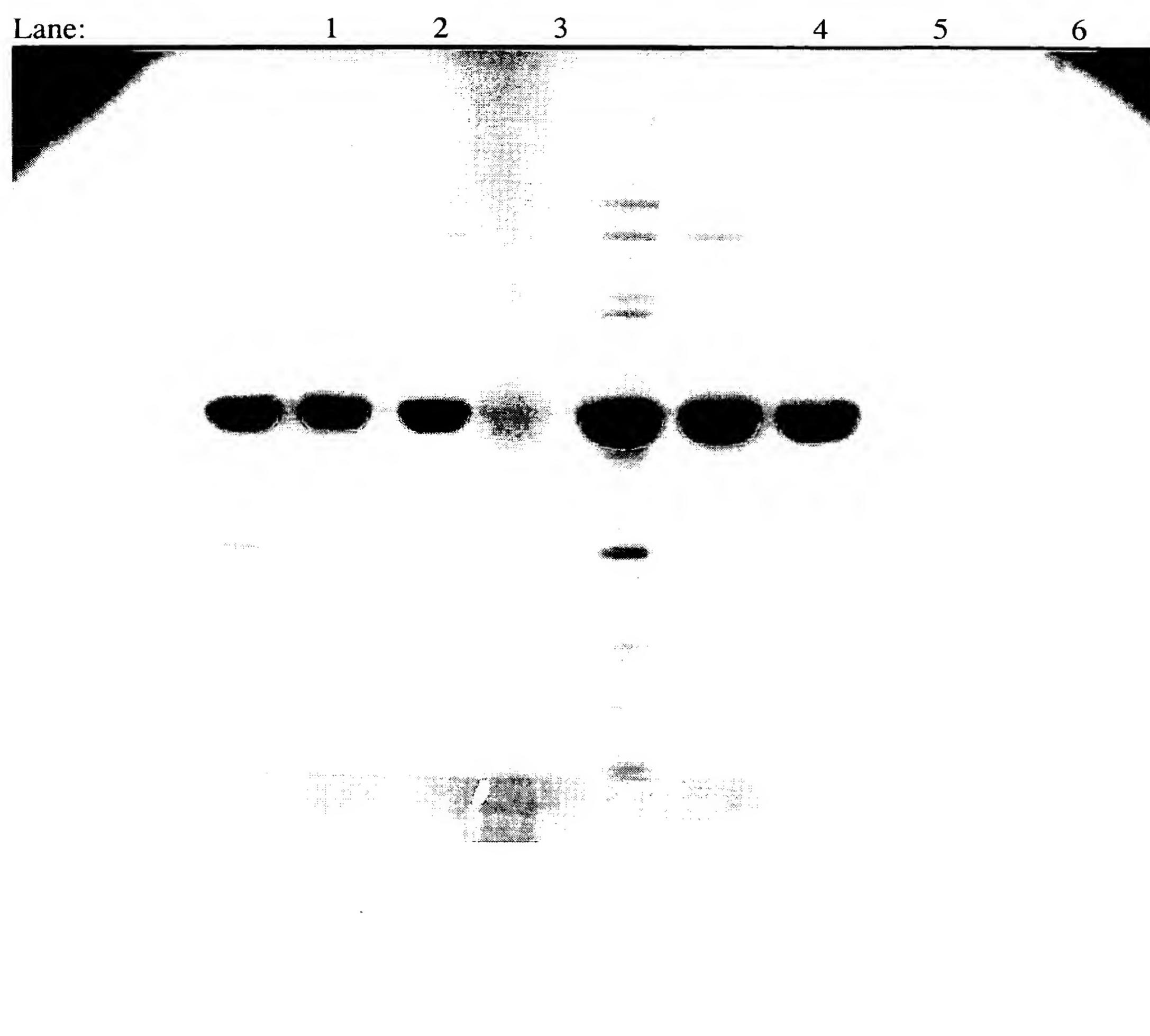
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Figure 5: SDS-PAGE showing expression of HAL in *E. coli*.



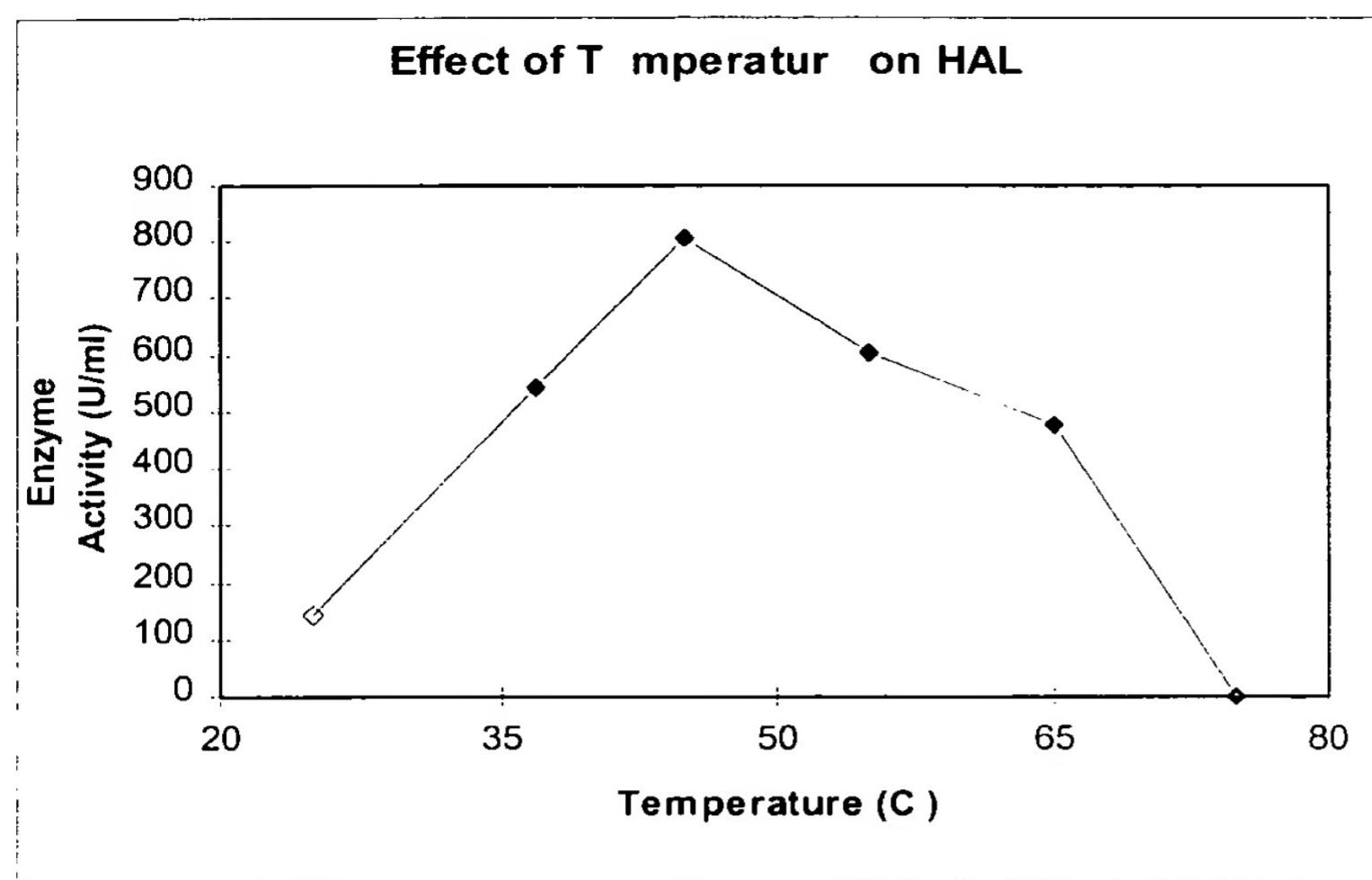
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Figure 6: SDS-PAGE showing purification of HAL from *E. coli*



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Figure 7: Effect of Temperature on HAL



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Figure 8: Effect of pH on HAL.

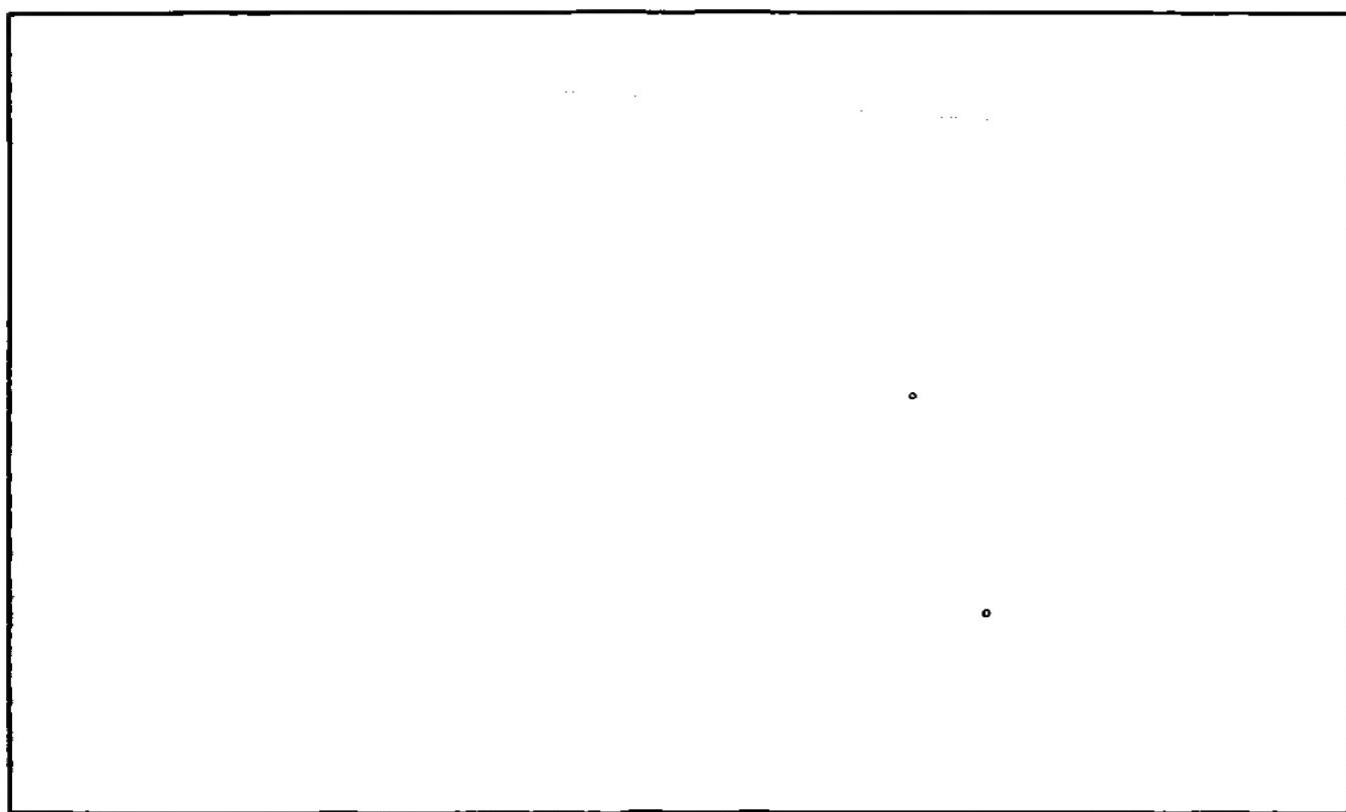
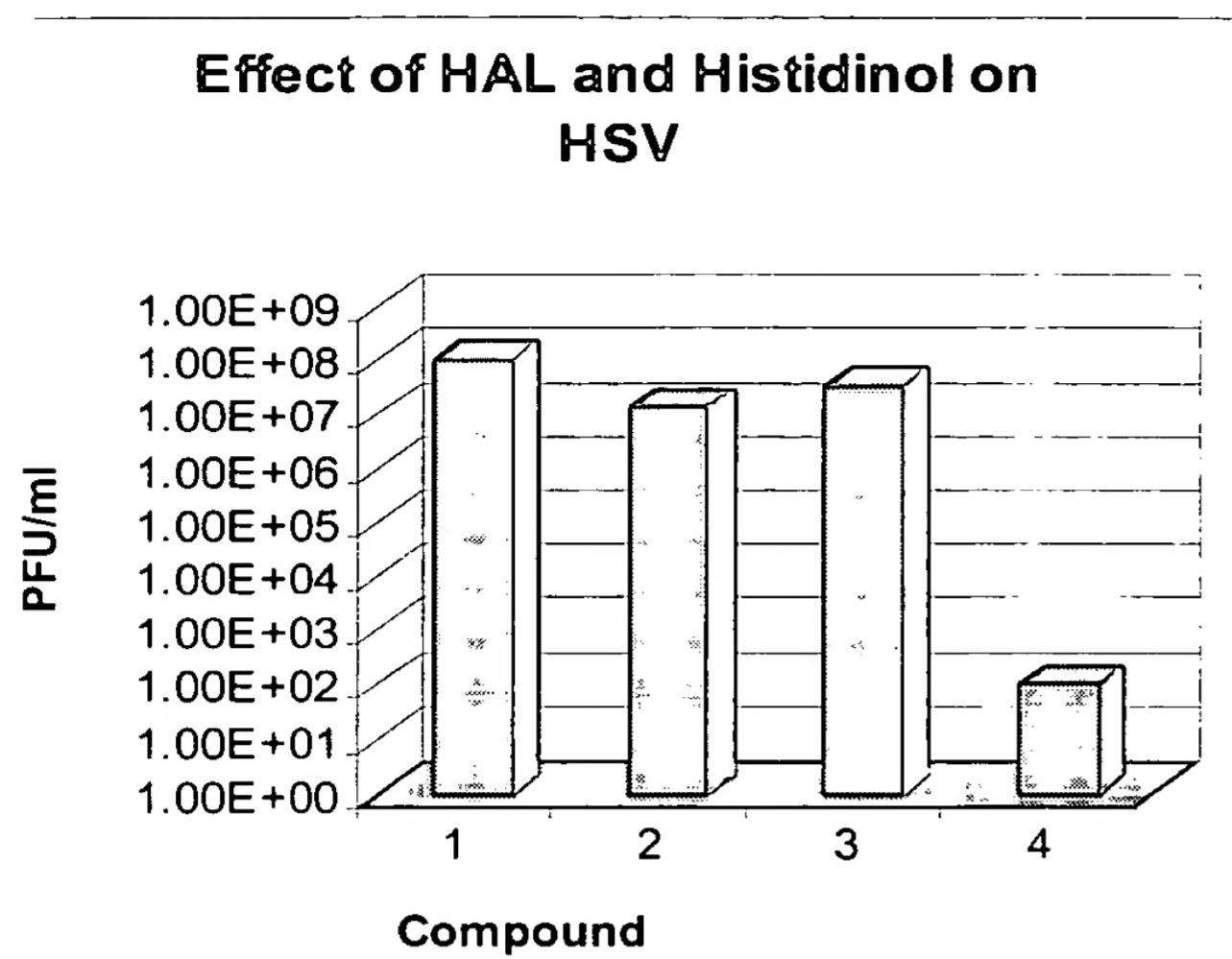


FIGURE 8
Effect of pH on HAL

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Figure 9: Effect of HAL and Histidinol on HSV.



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Figure 10: Effectiveness of L-histidinol as a Single Agent

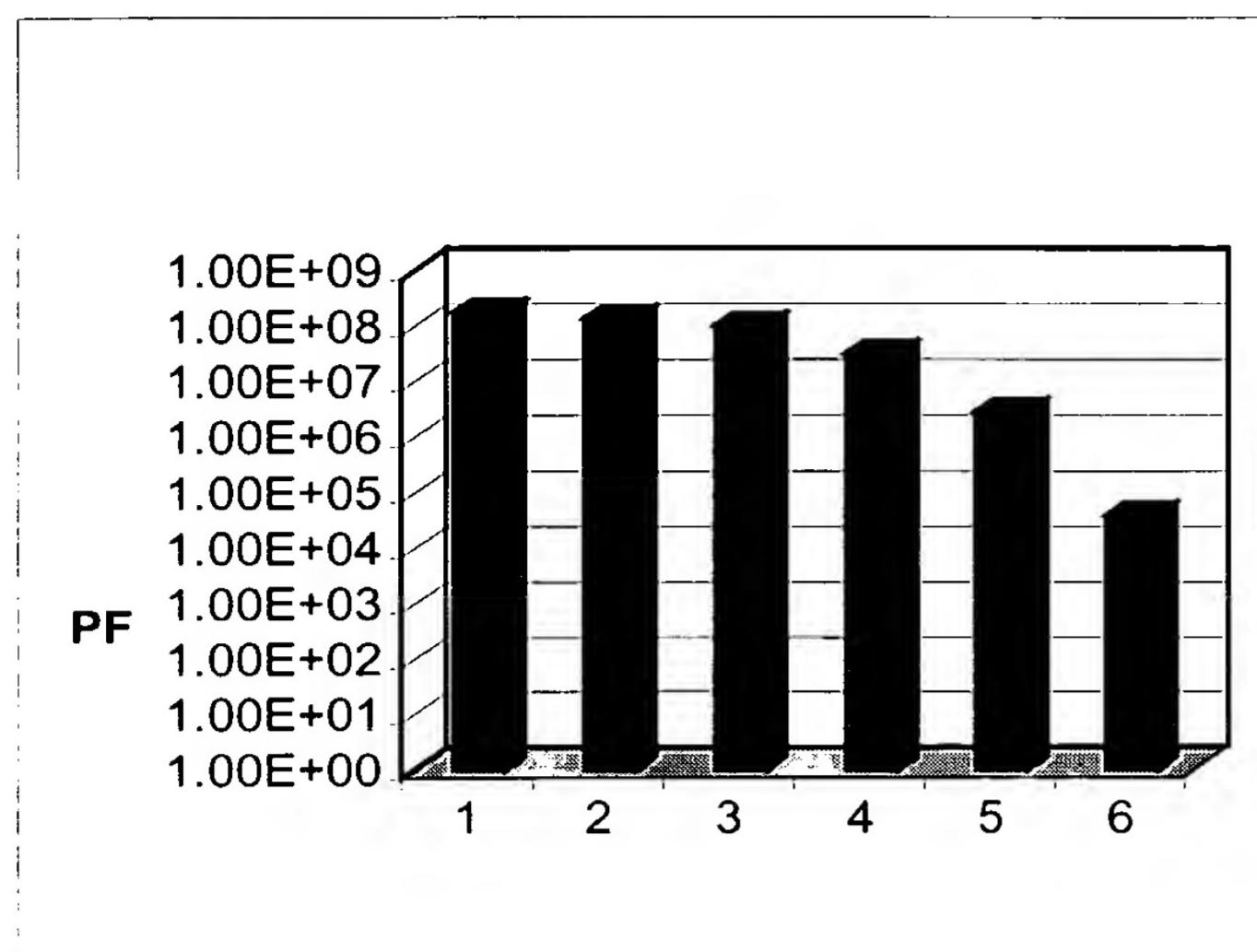
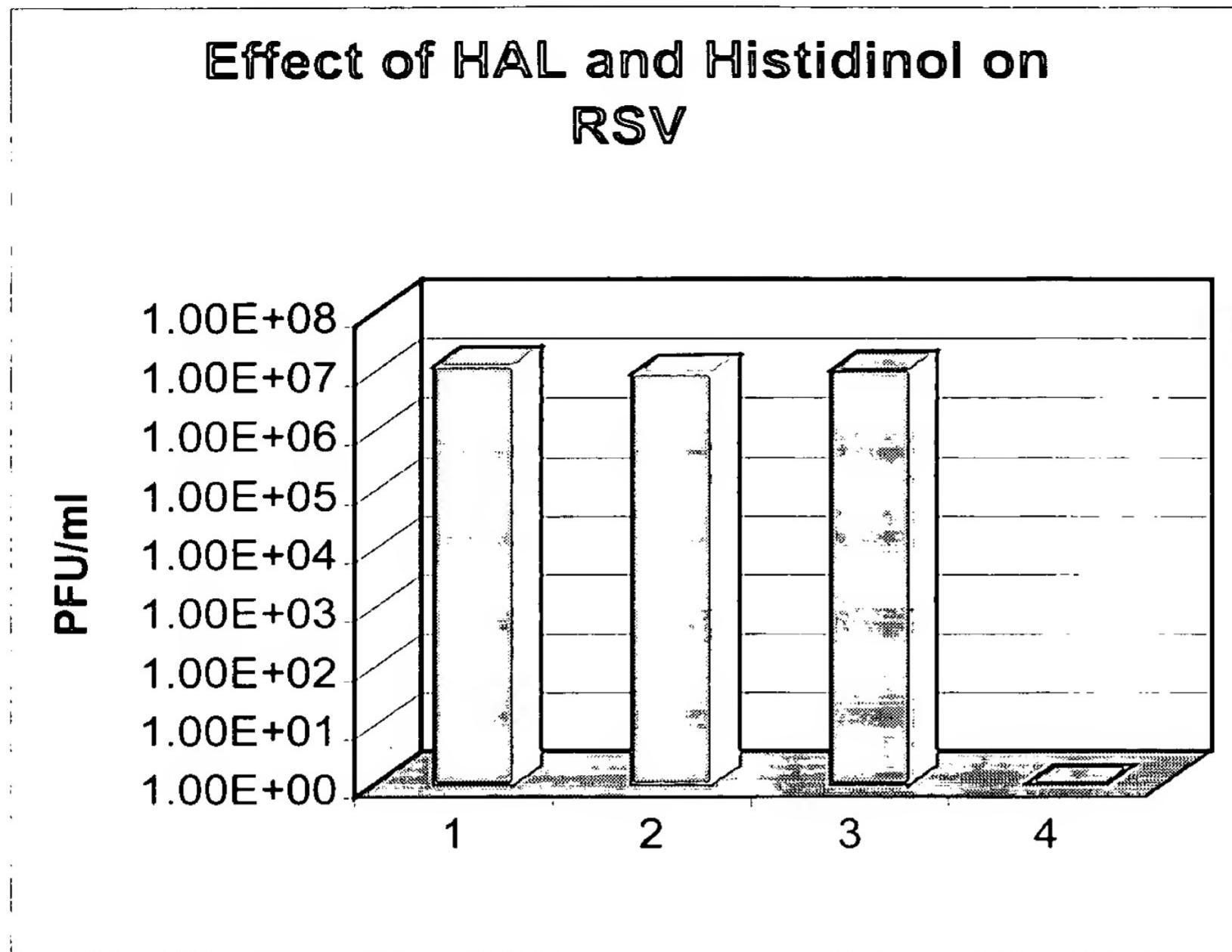


Figure 11: Effect of HAL and Histidinol on RSV.



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Figure 12: Effect of HAL on RMuLV.

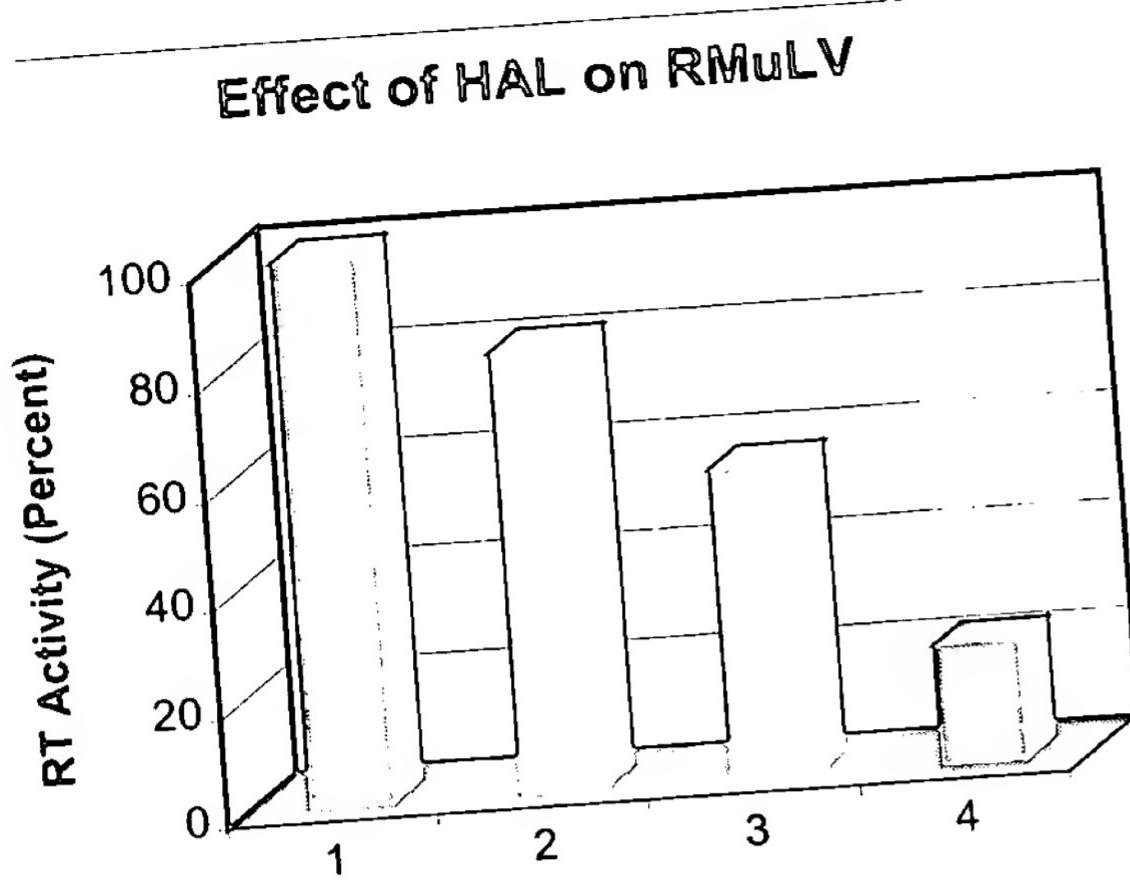


Figure 13: Histidine ammonia lyase peptide sequence pileup

HUTH_PSEPU -----
-
HUTH_RHIME -----
-
HUTH_MOUSE MPRYTVHVRGEWLAVPCQDGKLTGVWLGREAVRRYMKNPDNGGFTSVDEVQFLVHRCKG
HUTH_RAT MPRYTVHVRGEWLAVPCQDGKLSVGWLGREAVRRYMKNPDNGGFTSVDEVRFLVRRCKG
HUTH_HUMAN MPRYTVHVRGEWLAVPCQDAQLTVGWLGREAVRRYIKNKPDDAHFLVRRCKG
HUTH_CAEEL -MRLQVQIGTECVVVPCKP-DDTIHAVAKKSVEKLRLRPK-----
LPLADDYFEVRRTVG
HUTH_BACS -----
-
HUTH_STRGR -----
-
HUTH_CORY -----
-

□ HUTH_PSEPU -----
○ HUTH_RHIME -----
■ HUTH_MOUSE LGLLDNEDELEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
■ HUTH_RAT LGLLDNEDLLEVALEDNEFVEVVIEGDVMS-----PDFIPSQPEGVFLYSKYR---
△ HUTH_HUMAN LGLLDNEDRLEVALENNEFVEVVIEGDAMS-----PDFIPSQPEGVYLYSKYR---
* HUTH_CAEEL NSLLDPEDLVSDLKDSDFIIVAAASVEETEADAKEAKKQEEIDNARAEIEKIDNRRRKVSF
HUTH_BACS -----
* HUTH_STRGR -----
* HUTH_CORY -----
-

HUTH_PSEPU -----
TELTLKPGTLTLAQLRAIHAAPVRLQLDASAAPAIDASVACVEQIIA
HUTH_RHIME -----
MTVILRPGSVPLSLETIYWTGAPARLDAAFDAGIAKAAARIAEIVA
HUTH_MOUSE -----
EPEKYIALDGDSLSTEDLVNLGKGRYKIKLTSIAEKKVQQSREVIDSIIK
HUTH_RAT -----
EPEKYIALDGDSLSTEDLVNLGKGHYKIKLTSIAEKKVQQSREVIDSIIK
HUTH_HUMAN -----
EPEKYIELDGDRLTTEDLVNLGKGRYKIKLTPTAEKRVQKSREVIDSIIK
HUTH_CAEEL ADSLAPMVLAAPPTKLLILDGNSSLPEDLVRCEKGECAIQLSMESEDRIRKARTFLEKIAS
HUTH_BACS -----
MVTLDGSSLTTADVARVLDFEEAAASEESMERVKKSRAAVERIVR
HUTH_STRGR -----
MDMHTVVVGTSFTAEDVVAVARHARVELSAAAVEALAAARLIVDALAA
HUTH_CORY -----
MASAPQITLGLSGATAADDVIAVARHEARISISPQVLEELASVRAHIDALAS

Figure 13 cont'd.

HUTH_PSEPU EDRTAYGINTGFGLLASTRIASHDLENLQRSLVLSHAAGIGAPLDDDLVRLLMVIKINSL
HUTH_RHIME GNAPVYGINITGFGKLASIKIDSSDVATLQRNLILSHCCVGQPLTEDIVRLIMALKLISL
HUTH_MOUSE ERTVVYGITTGFGKFARTVIPANKLQELQVNLRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_RAT ERTVVYGITTGFGKFARTVIPANKLQELQVNLRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_HUMAN EKTVVYGITTGFGKFARTVIPINKLQELQVNLRSHSSGVGKPLSPERCRMLLALRINVL
HUTH_CAEEL EHRAVYGVTTGFGTFSNVTIPEKLLQLNLIRSHATGYGEPLAPNRARMLLALRINIL
HUTH_BACS DEKTIYGINTGFGKFSDVLIQEDSAALQLNLILSHACGVGDPFPECVSRAMLLLRLANAL
HUTH_STRGR KPEPVYGVSTGFGALASRHIGTELRAQLQRNIVRSHAAGMGPVEREVVRALMFLRLKTV
HUTH_CORY ADTPVYGIISTGFGALATRHIAPEDRAKLQRSLIRSHAAAGMGPVEREVVRALMFLRAKTL

HUTH_PSEPU SRGFSGIRRVIDALIALVNAEVYPHIPLKGSVGASGDLAPLATMSLVLLGEGKARYKGQ
HUTH_RHIME GRGASGVRLVRLIEAMLDKGVIPLIPEKGSVGASGDLAPLAHMAAVMMGHGEAFFAGE
HUTH_MOUSE AKGYSGISLETLKQVIEAFNASCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_RAT AKGYSGISLETLKQVIEVFNASCCLSYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_HUMAN AKGYSGISLETLKQVIEMFNASCLPYVPEKGTVGASGDLAPLSHLALGLIGEGKMWSPKS
HUTH_CAEEL AKGHSGISVENIKMIAAFNAFCVSYVPQQGTVGCSGDLCPHALALGLLGEGKMWSPTT
HUTH_BACS LKGFSGVRAELIEQLLAFLNKRVHPVIPQQGSLGASGDLAPLSHLALALIGQGEVFFEGE
HUTH_STRGR ASGHTGVRPEVAQTMADVLNAGITPVVHEYGSLGCSGDLAPLSHCALTMGEAEGPDG
HUTH_CORY ASGRS- VRPVVLETMVGMLNAGITPVVREYGSLGCSGDLAPLSHCALVLMGEATEDAHG

HUTH_PSEPU WLSATEALAVAGLEPLTLAAKEGLALLNTQASTAYALRGLFYAEDLYAAAACGGLSV
HUTH_RHIME RMKGDAALKAAAGLSPVTAAKEGLALINGTQVSTALALAGLFRAHRAGQAALITGALST
HUTH_MOUSE GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEALERASAIARQADIVAALT
HUTH_RAT GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALT
HUTH_HUMAN GWADAKYVLEAHGLKPIVLKPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALT
HUTH_CAEEL GWQPADVVLKKNNLEPLELGPKEGLALINGTQMITSLGCEAVERASAIARQADIVAALS
HUTH_BACS RMPAMTGLKKAGIQPVTLTSKEGLALINGTQAMTAMGVVAYIEAEKLAYQTERIASLT
HUTH_STRGR TVRPAGELLAHGIAPVELREKEGLALLNTDGMLGMLVMALADLRNLYTSADITAALSL
HUTH_CORY DIRPVPelfAEAGLTPVLAKEGLALVNGTDGMLGQLIMALADLDELLDIADATAAMSV

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Figure 13 cont'd.

HUTH_PSEPU EAVLGSRSPFDARIHE-ARGQRGQIDTAACFRDLLGDSSEVLSHKNCD----
KVQDPYS
HUTH_RHIME DAAMGSSAPFHPDIQH-CAAIRARSTRAALRQLTG-SPIRQSHIEGDE---
RVQDPYC
HUTH_MOUSE EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRCDRVQDAYT
HUTH_RAT EVLKGTTKAFDTDIHA-VRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRCDRVQDAYT
HUTH_HUMAN EVLKGTTKAFDTDIHA-LRPHRGQIEVAFRFRSLLDS-
DHHPSEIAESHRCDRVQDAYT
HUTH_CAEEL DVLKGTTRAYDPDIHR-IRPHRGQNLSALRLRALLHS-
EANPSQIAESHRNCKVQDAYT
HUTH_BACS EGLQGIIDAFDEDIHL-ARGYQEQQIDVAERIRFYLSD-SGLTTSQGE-----
LRVQDAYS
HUTH_STRGR EALLGTDKVLAPELHA-IRPHPGQGVSAVNMSRVLAG-SGLTGHHQDDAP---
RVQDAYS
HUTH_CORY EAQLGTDQVFRAELHEPLRPHPGQGRSAQNMFAFLAD-SPIVASHREGDG---
RVQDAYS

HUTH_PSEPU LRCQPQVMGACLTQLRQAAEVLGIEANAVSDNPLVFAAEGDVISGGNFHAEPVAMAADNL
HUTH_RHIME IRCQPQVDGACLDLLRSVAATLTIEANAVTDNPLVLSDN-
SVVSGGNFHAEPPVAFQADQI
HUTH_MOUSE LRCCPQVHGVVNDTIAFKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_RAT LRCCPQVHGVVNDTIAFKDIITTELNSATDNPMVFASRGETISGGNFHGEYPAKALDYL
HUTH_HUMAN LRCCPQVHGVVNDTIAFKNIITTELNSATDNPMVFANRGETVSGGNFHGEYPAKALDYL
HUTH_CAEEL LRCVPQVHGVVHDTIEFVREIITTEMNSATDNPLVFADREEIIISGGNFHGEYPAKALDFL
HUTH_BACS LRCIPQVHGATWQTLGYVKEKLEIEMNAATDNPLIFNDGDKVISGGNFHGQPIAFAMDFL
HUTH_STRGR VRCAPQVNGAGRDTLDHAALVAGRELASSVDNPVVLPDG-
RVESNGNFHGAPVAYVLDFL
HUTH_CORY LRCSPQVTGAARDTIAHARLVATRELAAAIDNPVVLPSC-
EVTSGNGNFHGAPVAYVLDFL

HUTH_PSEPU ALAIAEIGSLSERRIISLMMMDKHMS-
QLPPFLVENGGVNSGMIAQVTAALASENKALSH
HUTH_RHIME ALAVCEIGAIQRRIALLVDPALSLRLPAFLAKKPGLNSGLMIAEVTSALMSENKQLSH
HUTH_MOUSE AIGVHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGMIAHCTAAALVSESKALCH
HUTH_RAT AIGVHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGMIAHCTAAALVSESKALCH
HUTH_HUMAN AIGIHELAAISERRIERLCNPSLS-
ELPAFLVAEGGLNSGMIAHCTAAALVSESKALCH
HUTH_CAEEL AIAVAELAQMSERRLERLVNKELS-
GLPTFLTPDGGLNSGMFTVQLCAASLVSENKVLCH
HUTH_BACS KIAISELANIAERRIERLVNPQLN-
DLPPFLSPHPGLQSGAMIMQYAAASLVSENKTLAH
HUTH_STRGR AIVAADLGSICERRTDRLLDKNRSHGLPPFLADDAGVDGLMIAQYTQAALVSEMKR LAV
HUTH_CORY AIAVADLGSIAERRTDRMLDPARSRDLP AFLADDPGVDGMMIAQYTQAGLVAENKRLAV

Figure 13 cont'd.

HUTH_PSEPU PHSVDSLPTSANQEDHVSMAPAAGKRLWEMAENTRGVPATEWLGACQGLDLRKG-LKTS
HUTH_RHIME PASVDSTPTSANQEDHVSMAHCAGARRLLQMTENLFSIIGIEALAAVQGIEFRAP-LTTS
HUTH_MOUSE PSSVDSLSTSAAATEDHVSMMGGWAARKALRVVEHQVLAIELLAACQGIEFLRP-LKTT
HUTH_RAT PSSVDSLSTSAAATEDHVSMMGGWAARKALRVIEHQVLAIELLAACQGIEFLRP-LKTT
HUTH_HUMAN PSSVDSLSTSAAATEDHVSMMGGWAARKALRVIEHQVLAIELLAACQGIEFLRP-LKTT
HUTH_CAEEL PSSVDSIPTSCNQEDHVSMMGGFAARKALTVEAVLAMELLAACQGIEFLKP-LIST
HUTH_BACS PASVDSIPSSANQEDHVSMTIAARHAYQVIANTRRVIAIEAICALQAVEYRGI-EHAA
HUTH_STRGR PASADSIPIPSSAMQEDHVSMSGWSAARKLRTAVDNLARIVAVELYAAATRAIELRAAEGLTPA
HUTH_CORY PA-VDSIPIPSSAMQEDHVSMSGWSAARKLPTSVANLRRILAVEMLIAGRALDLRAP-LKPG

HUTH_PSEPU AKLEKARQALRSEVA-HYDRDRFFAPDIEKAVELLAGG---S-LTGLLPAGVLPSL---
-
HUTH_RHIME PELQKAAAARGVSS-SIEEDRYMADDLKAAGDLVASG---R-LAAAVSAGILPKLEN-
HUTH_MOUSE TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR
HUTH_RAT TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLLDQKVWEVAAPYIEKYRMEHIPESR
HUTH_HUMAN TPLEKVYDLVRSVVR-
PWIKDRFMAPDIEAAHRLLEQKVWEVAAPYIEKYRMEHIPESR
HUTH_CAEEL APLHKIYQLVRSVAP-
PLNEDRYMKPEIDAVLEMIREAHLPHLETLEAMEELDPD
HUTH_BACS SYTKQLFQEMRKVVVP-SIQQDRVFSYDIERLTDWLKK---ESLIPDHQNKELRGMNI-
HUTH_STRGR PASEAVVAALRAAGAEGPGPDRFLAPDLAADTFVREG---R-LVAAVEPVTGPLA---
-
HUTH_CORY PATGAVLEVLSRKVA-GPGQDRFLSAELEAAYDLLANG---S-VHKALE AHLPE----
-

HUTH_PSEPU -----
HUTH_RHIME -----
HUTH_MOUSE PLSPTAFSLESLRKNSATIPESDDL---
HUTH_RAT PLSPTAFSLESLRKNSATIPESDDL---
HUTH_HUMAN PLSPTAFSLQFLHKKSTKIPESEDL---
HUTH_CAEEL ALRQFTKTPTGIVQDRSMIPISDDEESIE
HUTH_BACS -----
HUTH_STRGR -----
HUTH_CORY -----

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Figure 14

Title: CLONING, OVEREXPRESSION AND
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HISTIDINE AMMONIA LYASE
Inventor(s): Joseph ROBERTS et al.
DOCKET NO.: 078728/0106

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Figure 14, cont'd.

		81	160
983831		100.0%	
1 SWALL: CAC21618		66.1%	RSLIRSHAAGMGEPVEREVVRALMFLRAKTLASGRTGVRPVVLETMVGMLNAGITPVVREYGLGCSGDLAPLISHCALVL
2 SWALL: HUTH_STRGR		65.4%	RNIVRSHAAGMGPVEREVVRALMFLRLKTVCSGRTGVRPEVAQTMADVLNAGITPVVHEYGLGCSGDLAPLISHCALTL
3 SWALL: HUTH_DEIRA		46.8%	RNIVRSHAAGMGPVEREVVRALMFLRLKTVASGHTGVRPEVAQTMADVLNAGITPVVHEYGLGCSGDLAPLISHCALLL
4 SWALL: BAB16159		42.0%	HNLIIVSHAIGMGEPLPAEVVRGMILLRAQSLSLGHSGVRVVEVVELLLAQNADALPVVPSQGSVGASGDLAPLAHLALGL
5 SWALL: Q9KWE4		42.0%	RNLILSHCCCGVGAAPLENVRLLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVIEPKGSVGASGDLAPLAHMSATM
6 SWALL: HUTH_BACSU		40.4%	RNLILSHCCCGVGAAPLENVRLLIMALKLISLGRGASGVRIELIRLIEGMLEKGVIPVIEPKGSVGASGDLAPLAHMSATM
7 SWALL: Q9KSQ4		42.2%	LNLILSHACGGVDPFPECVSRAMLLRLKGFSGVRAELIEQLLAFLNKRVHPVIFQQGSLGASGDLAPLISHLALAL
8 SWALL: Q9HU85		41.7%	KSIVLSHAAGIGEMLSDETVRLMMLKINSLARGSGIRLEVQALIELVNNQIYPCVPKKGSVGASGDLAPLAHMSLVL
9 SWALL: Q9KBE6		39.3%	RSIVLSHAAGVGEALDDAMVRLVMLLKVNSSLARGFSGIRRKVIDALIALINAEVYPHIPLKGSGVGASGDLAPLAHMSLVL
10 SWALL: HUTH_PSEPU		41.7%	HNLIYSHACGGVSPFPETVSRTMVLVRLLVRLNANALLKGESGVRPLVIERLLALVNANIIHPVIPQQGSLGASGDLAPLISHLALVL
11 SWALL: HUTH_RHIME		40.6%	RSLVLSHAAGIGAAMPLDDDLVRLINVLKINSLSRGFSGIRRKVVIDALIALVNAAEVYPHIPLKGSGVGASGDLAPLAHMAAVM
12 SWALL: Q9HU90		40.7%	RNLILSHCCCGVQQLTEDIVRLIMALKLISLGRGASGVRLVRLIEAMLDKGVIPLIKEPKGSVGASGDLAPLAHMSLVL
13 SWALL: HUTH_HUMAN		39.2%	RNTLLSHACGGVGEPLRDEQTRAIICAAVANYSQGKSGLDRSLVEGLLALLNHGITPQVPAQGSVGY---LTHMAHVGIAL
14 SWALL: HUTH_CAEEL		38.8%	VNLVRSHSSSGVGKPLSPERCMLLALRINVLAKGYSGISLETLKQVIEFNASCLSYVPEKGTGTVGASGDLAPLISHLALGL
15 SWALL: Q9HLT6		41.0%	LNLRSHATGYGEPLPNRARMLLALRINVLAKGYSGISVENIKKMAAFNAFCVSYYVQQGTVGCSGDLCPALAHIGLM
16 SWALL: HUTH_MOUSE		38.6%	KNLIRSHSSSGVGDYLENERYVRAIMAVRLNSLAAGYSAVSADLLNMMVEMLNRDVIPAVEFKYGSVGASGDLAPLISHLALGL
17 SWALL: BAB29407		38.6%	VNLVRSHSSSGVGKPLSPERCMLLALRINVLAKGYSGISLETLKQVIEFNASCLSYVPEKGTGTVGASGDLAPLISHLALGL
18 SWALL: HUTH_RAT		38.2%	VNLVRSHSSSGVGKPLSPERCMLLALRINVLAKGYSGISLETLKQVIEVENASCLSYYVPEKGTGTVGASGDLAPLISHLALGL
19 SWALL: AAG53586		39.8%	RSLVLSHAAGVGEPLDDDIVRLMMVLKINSLARGFSGIRLSVIAQALIALVNAGVSYVDPAKGSVGASGDLAPLAHMSLTL
20 SWALL: Q9KKE0		38.9%	RNIILSHACGGVGDPLGRVEARVMAAQIANLTHGYSGVRVETAEMLLAQNADILPLIPSRSGSVGY-----LTHAALVL
21 SWALL: Q9HQD5		42.2%	ANLVRSHAGAGSELDTAAVRALLVTRLNALAKGYSGIRERVLDVLVGLLNEGVHPVVPSRGSLGASGDLAPLAHMSRVL

Figure 14, cont'd.

		161	240
983831		100.0%	
1 SWALL: CAC21618		66.1%	MGEGEATDAHGDIRPVPELFAEAGLTPEVLAKEEGGLALVNNTDGMLGQLIMALADLDELLDIADATAAMSVEAQLGTDQV
2 SWALL: HUTH_STRGR		65.4%	MGEGDAEGPDGTVRPAGELLAAHGTAPVELREKEGLALLNCTDGMLGMLVMAADLDLTLYKSADIITAALTMEALLGTDKV
3 SWALL: HUTH_DEIRA		46.8%	IGLGDI-EYQQVVRPAADVLAELGLSPVQLQAKEGLLINGTQLMGSLLALHDAQVLGLTANLAAMTVEARYGSHRP
4 SWALL: BAB16159		42.0%	MGEGEAF-YQGVQMPSKDALAKAGISPVVLAKEGLALINGQTSTALALAGIFRAHRAQSALVTGALISTDAAMGSASP
5 SWALL: Q9KWE4		42.0%	IGQGEAF-YQGVQMPSKDALAKAGISPVVLAKEGLALINGQTSTALALAGIFRAHRAQSALVTGALISTDAAMGSASP
6 SWALL: HUTH_BACSU		40.4%	IGQGEVF-FEGERMPAMTGLKKAGIQPVTLTSKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAYQTERIASLTIEGLQGIIDA
7 SWALL: Q9KSQ4		42.2%	LGEQAR-YNGKILSGLEAMKIAGLEPTILAPKEGLALLNGTQASTAFALEGLFVAEDLFASATVCGAMSVEAALGSRRP
8 SWALL: Q9HU85		41.7%	IGESRARH-RGEWLPAAEALAVAGLEPLTLAAKEGLALLNGTQVSTAYALRGFLFEAEDLFAAATVCGGLSVEAAMLGSRAP
9 SWALL: Q9KBE6		39.3%	LGEGEVF-YKGTKTKASFALKEEIEPITLTAKEGLALLNGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
10 SWALL: HUTH_PSEPU		41.7%	LGEKAR-YKGQWL.SATEALAVAGLEPLTLAAKEGLALLNGTQASTAYALRGFLFYAEDLYAAAIACGGLSVEAVLGSRSP
11 SWALL: HUTH_RHIME		40.6%	MGHGEAFFAGERMKGDAALK-AGLSPVTLAAKEGLALLNGTQVSTAYALRGFLFYAEDLYAAAIACGGLSVEAVLGSRSP
12 SWALL: Q9HU90		40.7%	LGIGEV-S-YRGSVVVPAAAALAAEGLATVRLGAKDGLCLVNGTPCMTGACLAQDAQRLAQWADVIGAMSFEALRGQIAA
13 SWALL: HUTH_HUMAN		39.2%	VGEGMWSPKSGWADAKYVLEAHGLKPVILPKKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
14 SWALL: HUTH_CAEEL		38.8%	LGEKMMWSPTTGWQPADVVLKKNNPLELPKKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
15 SWALL: Q9HLI6		41.0%	MGEGKAF-FEGRLMDSARALEKAGLKPYQFKEKEGVALINTSFMSGILSIAVMDAHDILENAIRSALLSEALGGTSKA
16 SWALL: HUTH_MOUSE		38.6%	IGEGKMMWSPKSGWADAKYVLEAHGLKPVILPKKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
17 SWALL: BAB29407		38.6%	IGEGKMMWSPKSGWADAKYVLEAHGLKPVILPKKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
18 SWALL: HUTH_RAT		38.2%	IGEGKMMWSPKSGWADAKYVLEAHGLKPVILPKKEGLALINGTQAMTQAMTGAQSLVYIEAEKLAQFQSEIIIASLTMEGLRGIDI
19 SWALL: AAG53586		39.8%	LGEKAR-YRGEWLPAATALQKAGLAPVTLAAKEGLALLNGTQASTAFALRGFLFEAEDLFASAVVCGALTTEAVLGSRP
20 SWALL: Q9KKE0		38.9%	IGHGSAMQGTERLSGADAL-ARLGLAPLRLREAKEGLSLVNNTPCATGLAALALARTEFLFAWADAAMTYE-NLGQSAN
21 SWALL: Q9HQD5		42.2%	IGEGQA-DVAGERMPAAEALAAFADLEPVTLQAKEGLALINGTQLTGVAALALVDAERVLSADTAGALTTEVTMSTAS

Title: CLONING, OVEREXPRESSION AND
THERAPEUTIC USE OF BIOACTIVE
HISTIDINE AMMONIA LYASE
Inventor(s): Joseph ROBERTS et al.
DOCKET NO.: 078728/0106

Figure 14, cont'd.

U.S. Patent and Trademark Office

		241	3	320
983831		100.0%		
1 SWALL: CAC21618		66.1%	LAPELHA-IRPHPGQAAASAAANMAAVLKGSGLTGHHQDDAPRVRQDAYSVRCAPQVAGAGRDTMAHAGLVAERELAAVIDNPLAPELHA-IRPHPGQGVSDNMSRVLAGSGLTGHHQDDAPRVRQDAYSVRCAPQVNGAGRDTLDHAALVAGREIASSVDNPFQPDV-VGLRPHPGALAVAAELREFFLAGSEIAPSHLTGDGVQDAYSLRAVPOVHGATWQDQVHGAQCLDLSAVERVLAVEFASVTDNPFHPDIHT-LRGHKKGQIDAGSSALRNLLQGSEIRESHIEGDERVQDPYCIRCQCPQVHDGACLQDLSAVERVLAVEFASVTDNPFHPDIHT-LRGHKKGQIDAGSSALRNLLQGSEIRESHIEGDERVQDPYCIRCQCPQVHDGACLQDLSAVERVLAVEFASVTDNPFDEDIHLA-RGYQEQQIDVAERIRFYLSDGLTTS--QGELRVQDAYSLRClPOVHGATWQTLGYVVKERLEIEMNAATDNPFDPRIHR-VRGHRTQMADAATAYRHLLVSSEIGQSHNSNE-KVQDPYSLRCQCPQVMGACLQQIRSAAEVLEVEANSVSNDNFDARIHAA-RGQRGQIDVAAYRDLLASSEVARSHENKCD-KVQDPYSLRCQCPQVMGACLTQMRQAEEVLEIEANAVSNDNFDEQIHFA-RGYVEQVQDVARRMESYLQDSQLTT--RQGELRVQDAYSLRClPOVHGATWQTLRYVVKERLEIEMNAATDNPFDARIHE-RGQRGQIDTAACFRDLIGDSSEVSSSHRNCD-KVQDPYSLRCQCPQVMGACLTQLRQAEEVLGIEANAVSNDNFHPDIQHCAAIRARSTRAAA-LRQLLTGSPIRQSHIEGDERVQDPYCIRCQCPQVHDGACLQDLSAVERQHARQIET-ELNSATDNPFDAE1-VALKPHPGMQRVAANLRLALLAGSQVLENAR--GIRTQDALSIERSIPQIHGACRDQLAHARQIET-ELNSATDNPFDTDIHA-LRPHRGQIEVAFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKNIITTELNSSATDNPYDPDIHR-IRPHRGQNLISALRLALLNPSQIAESHRNCT-KVQDAYTLRCCPQVHGVVHDTIEFVREIITTEMNSATDNFFTPWILGA-RPHLGQVAIGNRFREYLTGSDIV--KRADSVKQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSSVIEINSATDNPFDTDIHA-VRPHRGQIEVAFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSSATDNPFDTDIHA-VRPHRGQIEVAFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSSATDNPFDTDIHA-VRPHRGQIEVAFRSLLSDSEIAESHRFCD-RVQDAYTLRCCPQVHGVVNDTIAFVKDIITTELNSSATDNPFDARIHE-VRGQRGQIDAAALFRHVLTDTSAIASHHNCD-KVQDPYSLRCQCPQVMGACLTQMRQVAEVLLVESNAVSNDNPAFAELPLALRQSPGGLSAVGEGLRDWLADSMFLAG-TAGTRTQDPLSLRAVPOVHGAAARDAFGQVAEVDRRELASVTDNPCAPAHE-VRPHDGQAVSARHIRNLTAGSEVLDHHRDCD-RVQDAYSIIRCLPQVHGAVRDALDHRAAVATELNSSATDNP	
1 SWALL: HUTH_STRGR		65.4%		
3 SWALL: HUTH_DEIRA		46.8%		
4 SWALL: BAB16159		42.0%		
5 SWALL: Q9KWE4		42.0%		
6 SWALL: HUTH_BACSU		40.4%		
7 SWALL: Q9KSQ4		42.2%		
8 SWALL: Q9HU35		41.7%		
9 SWALL: Q9KBE6		39.3%		
10 SWALL: HUTH_PSEPU		41.7%		
11 SWALL: HUTH_RHIME		40.6%		
12 SWALL: Q9HU90		40.7%		
13 SWALL: HUTH_HUMAN		39.2%		
14 SWALL: HUTH_CAEEL		38.8%		
15 SWALL: Q9HLI6		41.0%		
16 SWALL: HUTH_MOUSE		38.6%		
17 SWALL: BAB29407		38.6%		
18 SWALL: HUTH_RAT		38.2%		
19 SWALL: AAG53586		39.8%		
20 SWALL: Q9KKE0		38.9%		
21 SWALL: Q9HQD5		42.2%		

Title: CLONING, OVEREXPRESSION AND
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HISTIDINE AMMONIA LYASE
Inventor(s): Joseph ROBERTS et al.
DOCKET NO.: 078728/0106

Figure 14, cont'd.

		321	400
983831		100.0%	VVLPSGEVTSNGNFHGVAYVLDLAIAVADLGSTIAERRTDRLMLDPARSRDLPFLAFLADDPGVDGGMMIAQYQTQAGLVAE
1 SWALL:CAC21618		66.1%	VVLPDGRVESNGNFHGVAYVLDLFLAVAVADLGSTIAERRTDRLMLDKNRSHGLLPFLADDAGVDDGFLPFLADDAGVDTNPA
2 SWALL:HUTH_STRGR		65.4%	LIFPTGEVVSGGNFHGVPLAVTIDALKVAEALGSICERRTDRLMLDKNRSHGLLPFLADDAGVDTNPA
3 SWALL:HUTH_DEIRA		46.8%	LVLSDNSVVSQGNFHGVPLAVTIDALKVAEALGSICERRTEQLLNPA
4 SWALL:BAB16159		42.0%	LVLSDNSVVSQGNFHGVPLAVTIDALKVAEALGSICERRTEQLLNPA
5 SWALL:Q9KWE4		42.0%	LIFNDGDVVISGGNFHGQPIAFAMDFLKIAISELANIAERRIERLVNPQLN-DLPPFLSPHPGLQSGAMIMQYAAASLVSE
6 SWALL:HUTH_BACSU		40.4%	LVFADGDIISGGNFHAEPVAMAADNLALIAEIGSLSERRMALLIDSALK-LFPEFLVNDGGVNSGFMIAQVTTAAALASE
7 SWALL:Q9KSQ4		42.2%	LVFAAGDVVISGGNFHAEPVAMAADNLALIAEIGSLSERRMALLIDSALK-LFPEFLVNDGGVNSGFMIAQVTTAAALASE
8 SWALL:Q9HU85		41.7%	LIFDNGQVISGGNFHGQPIAFAMDFLKIAISELANIAERRIERLVNPQLN-DLPPFLSAAPGVQSGVMILQYCAASLVSE
9 SWALL:Q9KBE6		39.3%	LVFADGDIISGGNFHAEPVAMAADNLALIAEIGSLSERRMALLIDSALK-LFPEFLVNDGGVNSGFMIAQVTTAAALASE
10 SWALL:HUTH_PSEPU		41.7%	LVLSDNSVVSQGNFHGVPLAVTIDALKVAEALGSICERRISLMMMDKHMMSQ-LFPEFLVNDGGVNSGFMIAQVTTAAALASE
11 SWALL:HUTH_RHIME		40.6%	LLLGTPEVVSQANPHGESVAMAADDLLAIAEVLLGVAERRLDRLVNPILVS-GLPAFLVGRPGVNVSGMMITQYVAASLAGE
12 SWALL:Q9HU90		40.7%	MVFANGETVSGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-ELPAFLVAGGLNNSGFMIAHCTAAALVE
13 SWALL:HUTH_HUMAN		39.2%	LVFADREIIISGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-GLPFLTLPDGGLNNSGFMVTQVLCAAASLVSE
14 SWALL:HUTH_CAEEL		38.8%	L-ENGEEVVSGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-GLGNMVERRIARLVDTNLS-GLPAFLVAGGLNNSGFMIAHCTAAALVE
15 SWALL:Q9HL16		41.0%	MVFASGETISGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-ELPAFLVAGGLNNSGFMIAHCTAAALVE
16 SWALL:HUTH_MOUSE		38.6%	MVFASGETISGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-ELPAFLVAGGLNNSGFMIAHCTAAALVE
17 SWALL:BAB29407		38.6%	MVFASGETISGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-ELPAFLVAGGLNNSGFMIAHCTAAALVE
18 SWALL:HUTH_RAT		38.2%	MVFASGETISGGNFHGEYPAKALDYLAIGTHELAASIERRIERLCNPSLS-ELPAFLVAGGLNNSGFMIAHCTAAALVE
19 SWALL:AAG53586		39.8%	LVFAANEMVFRGNFHAEPVAMAADNLALIAEIGALSERRIALMMMDKHMMSQ-LFPEFLVNRGGVNSGFMIAQVTTAAALASE
20 SWALL:Q9KKE0		38.9%	AVAGSPEVHSQAHAVGAALGLANDSLAVAVAEEVAISERRRIDRLVNPILVS-GLPAFLAGDSGVSSGFMIAQYTTAAALVAE
21 SWALL:Q9HQD5		42.2%	LVFPSGTVVSGGNFHGEVLAIRLYGAASALAEAAISERRRTDRLLNPETQEPLEPFLAPDSGLHSGLMIPQYTTAAASLVND

Figure 14, cont'd.

	401
983831	100.0%
1 SWALL: CAC21618	66.1%
2 SWALL: HUTH_STRGR	65.4%
3 SWALL: HUTH_DEIRA	46.8%
4 SWALL: BAB16159	42.0%
5 SWALL: Q9KWE4	42.0%
6 SWALL: HUTH_BACSU	40.4%
7 SWALL: Q9KSQ4	42.2%
8 SWALL: Q9HU85	41.7%
9 SWALL: Q9KBE6	39.3%
10 SWALL: HUTH_PSEPU	41.7%
11 SWALL: HUTH_RHIME	40.6%
12 SWALL: Q9HU90	40.7%
13 SWALL: HUTH_HUMAN	39.2%
14 SWALL: HUTH_CAEEL	38.8%
15 SWALL: Q9HLI6	41.0%
16 SWALL: HUTH_MOUSE	38.6%
17 SWALL: BAB29407	38.6%
18 SWALL: HUTH_RAT	38.2%
19 SWALL: AAG53586	39.8%
20 SWALL: Q9KK0	38.9%
21 SWALL: Q9HQD5	42.2%

NRLLAVPASVDSIPSSAMQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
LKRLAVPASADSIPSSAMQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
MKRLAVPASADSIPSSAMQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKVLSPHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKQMSHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKQMSHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKTLAHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKTLAHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKTLAHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKALAHPSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKTLAHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKALSHPHSPVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKQI, SHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKQI, SHPASVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NRQLAQPAVVDNFVTSALQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKALCHPSSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKVLCHPSSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKVLAYPSSADTIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
SKALCHPSSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
SKALCHPSSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NKGLCHPSSVDSIPTSANQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
NRLLAAPASLDGGITSAQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG
LRSLGQP-TLDNASVSGAQEDHVSIGRALDLRAPLKGCPATGAVLEVLSKVAG

Figure 14, cont'd.

		481
983831		100.0%
1 SWALL: CAC21_618		66.1%
2 SWALL: HUTH_STRGR		65.4%
3 SWALL: HUTH_DEIRA		46.8%
4 SWALL: BAB1_6159		42.0%
5 SWALL: Q9KWE4		42.0%
6 SWALL: HUTH_BACSU		40.4%
7 SWALL: Q9KSQ4		42.2%
8 SWALL: Q9HU85		41.7%
9 SWALL: Q9KBE6		39.3%
10 SWALL: HUTH_PSEPU		41.7%
11 SWALL: HUTH_RHIME		40.6%
12 SWALL: Q9HU90		40.7%
13 SWALL: HUTH_HUMAN		39.2%
14 SWALL: HUTH_CAEEL		38.8%
15 SWALL: Q9HLI6		41.0%
16 SWALL: HUTH_MOUSE		38.6%
17 SWALL: BAB2_9407		38.6%
18 SWALL: HUTH_RAT		38.2%
19 SWALL: AAG5_5586		39.8%
20 SWALL: Q9KKE0		38.9%
21 SWALL: Q9HQD5		42.2%

[5 . . .] 513

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PGQDREFL SAELEAA YDL LANG SVHKALEAH LPA
PGPDRH LAPDLA AADAFV RAGHLV AAAESVTGP
PGPDRFLAPDLAAADTFVREGRLVAAVEPV TGP
LTEDRYFRPDLLR LRGE LVSGRV AQA ADTQAPA
LEDDRYMATDLKA AIEV VAS GALVSA ISSGLPV
LEDDRYMATDLKA AIEV VAS GALVSA ISSGLPV
IQQDRVFSYDIERLTDW LKKESLIPDHQNKELR
YDKDRYFAPDIE KANAL L-QLA VHNRLMPDQLL
YQEDRFFAPDIE AASQL LASGCLN ALLPARLLP
IDQDRMFAK DIERA AAKWLKDGSWDFTKMREKER
YDRDRFFAPDIE KAV ELLAKGS LTG LIPAGLPS
IEEDRYMADDLKA AGDLV ASGRLAA AVSAGL PK
YDTDWR LAPI DIAAAA IILGERKS LARLA ASIGD
WIKDRFMAPDIE AAHRL LLEQK VWEVAAPYIEK
PNEDRYMKPE IDAVLEMIRENR IWEAVLPHLET
LDHD RPPSF DIELTIRKMDKKEFISALP-----.
WIKDRFMAPDIE AAHRL LLDQKVWEVAAPYIEK
WIKDRFMAPDIE AAHRL LLDQKVWEVAAPYIEK
YDDDRFFAPDIE AAISL NKGSLV GLLP AFL--.
PIATIVR-----.
PAGDRAL ADDMAAV GDL VRAGL VEDA VAR ALDA

```

Figure 14, cont'd.

KEY:

983831	:	HAL
1	CAC21618	: Streptomyces coelicolor
2	HUTH_STRGR	: Streptomyces griseus
3	HUTH_DEIRA	: Deinococcus radiodurans
4	BAB16159	: Agrobacterium rhizogenes
5	Q9KWE4	: Agrobacterium rhizogenes
6	HUTH_BACSU	: Bacillus subtilis
7	Q9KSQ4	: Vibrio cholerae
8	Q9HU85	: Pseudomonas aeruginosa
9	Q9KBE6	: Bacillus halodurans
10	HUTH_PSEPU	: Pseudomonas putida
11	HUTH_RHIME	: Rhizobium meliloti
12	Q9HU90	: Pseudomonas aeruginosa
13	HUTH_HUMAN	: Human
14	HUTH_CAEEL	: Caenorhabditis elegans
15	Q9HLI6	: Thermoplasma acidophilum
16	HUTH_MOUSE	: Mouse
17	BAB29407	: Mus musculus (Mouse)
18	HUTH_RAT	: Rat
18	AAG53586	: uncultured bacterium pCosAS1
20	Q9KKE0	: Rhizobium meliloti
21	Q9HQD5	: Halobacterium sp

Title: CLONING, OVEREXPRESSION AND
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HISTIDINE AMMONIA LYASE
Inventor(s): Joseph ROBERTS et al.
DOCKET NO.: 078728/0106

Figure 15

Title: CLONING, OVEREXPRESSION AND
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HISTIDINE AMMONIA LYASE
Inventor(s): Joseph ROBERTS et al.
DOCKET NO.: 078728/0106

Figure 15, Cont'd.

STRG	365	KNRSHGLPPFLADDAGVDSGLMIAQYTQAALVSEM KRI LAVP A SSADSI PSSAM QEDHVSMG	
HAL	367	PARSRDLPAFLADDPGVDSGMMIAQYTQAGLVAEN KRI LAVP A SSVDSI PSSAM QEDHVSLG	* * * * *
STRG	425	WSAARKLRTAVDNLARI V AVELYAA T RAIELRAAEG G LP G GP	
HAL	427	WHAARKLRTSVANL R RI L AVEM L IAGR A LDLRAP--LKPGPATGAVLEV L RSKVA-GPGQ	* * * * *
STRG	485	DRF L APD L AA A DTF V REG R ILVAAVE	
HAL	484	DRF L SAE L EA Y DLANGSVHKALE	* * * *